DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the experimental design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. DO NOT EXCEED THE SPACE PROVIDED.

Ovarian cancer (OV Ca) has the highest rate of mortality among all gynecologic cancers and the major forms of OV Ca originate from the cells of the surface epithelium of the ovary. Embryologically cells of the surface epithelium also give rise to at least part of the granulosa cells. The most important regulatory hormones which control functions of the ovarian granulosa and theca/stromal (ST) cells are the gonadotropins and estradiol secreted by follicle cells. The gonadotropins (LH and FSH) may directly, or through ovarian steroid or growth factor production, promote the transformation and control the resulting neoplastic behavior of the surface epithelial cells leading to epithelial OV Ca. Previously the human LH/hCG receptor (LH/hCG R) was purified, monoclonal antibodies were raised against purified rat LH/hCG R, and steroid secreting OV Ca cells were cultured.

Specific aim one is to clone the human LH/hCG R complimentary DNA (cDNA). By using mRNA from human corpora lutea, a cDNA library has been synthesized. Oligonucleotide probes and mAb against LH/hCG receptor will be used to identify the receptor cDNA; the latter will be amplified and expressed in LH/hCG R minus OV Ca cells to study whether LH/hCG can regulate growth rates and metabolic functions in transfected OV Ca cells.

Specific aim two is to develop a mAb against the purified human LH/hCG R with the long-term goal of developing a mAb-daunomycin conjugate which can deliver daunomycin specifically to OV Ca cells, since LH/hCG R is found only in ovarian cells. OV Ca cells may have normal or altered LH/hCG R; this will be determined by the use of mAb and polyclonal antipeptide Ab against LH/hCG R and hormone binding. Polyclonal Ab will be raised in rabbits against predicted amino acid sequences of LH/hCG R. The metabolic and antiproliferative effects of mAb and polyclonal mAb on OV Ca cells in culture and OV Ca cells growing in a nude mouse model will be studied.

The third specific aim is to expand work on optimizing conditions for OV Ca cell growth and to conduct detailed studies on the growth and metabolic responses of these cells to gonadotropins and gonadotropin-releasing hormone and growth factors.

The fourth specific aim is to develop an antipeptide antibody to the FSH receptor based on the rat putative FSH receptor sequence and to test its effects on human granulosa and ST cells and OV Ca cell metabolism and growth rates.

KEY PERSONNEL ENGAGED ON PROJECT

NAME, DEGREE(S), SSN	POSITION TITLE AND ROLE IN PROJECT	DEPARTMENT AND ORGANIZATION
Jayantha Wimalasena, Ph.D. [redacted]	Assistant Professor Principal Investigator	University of Nebraska College of Medicine Physiology and Biophysics Department
G. Stanley Cox, Ph.D. [redacted]	Associate Professor Co-Investigator	University of Nebraska College of Medicine Biochemistry Department
Donald Johnson, Ph.D. [redacted]	Associate Professor Co-Investigator	University of Nebraska College of Medicine Pathology and Microbiology Department
McClure Smith, M.D. [redacted]	Professor and Chairman	University of Nebraska College of Medicine Obstetrics & Gynecology Department